

South East London glucagon-like peptide (GLP-1) analogue pathway for adults aged 18 years and over with Type 2 Diabetes Mellitus (T2DM).

This guidance does NOT override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

Developed by the SEL Diabetes Medicines Working Group on behalf of the South East London Integrated Medicines Optimisation Committee

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South East London Integrated Medicines Optimisation Committee (SEL IMOC). A partnership between NHS organisations in South East London Integrated Care System: NHS South East London (covering the boroughs of Bexley/Bromley/Greenwich/ Lambeth/Lewisham and Southwark) and GSTFT/KCH /SLaM/ Oxleas NHS Foundation Trusts and Lewisham & Greenwich NHS Trust

Flowchart 1) Access to GLP-1 analogues – including GLP-1 receptor agonists (GLP-1 RAs) and joint GLP-1 RA and Glucose-dependent Insulinotropic Polypeptide (GIP) agonists in South East London

Management of type 2 diabetes (T2DM)

Patient meets the following criteria:

If triple therapy with metformin and 2 other oral anti-hyperglycaemic drugs is not effective, not tolerated or contraindicated, consider triple therapy by switching one drug treatment to a GLP-1 RA/Joint GLP-1 RA and GIP agonist – see [T2DM Glycaemic Control Management Pathway](#) in those whom:

- BMI $\geq 35\text{kg/m}^2$ (adjust accordingly for ethnicity) and specific psychological or other medical problems associated with obesity **OR** BMI $< 35\text{kg/m}^2$ and where insulin would have significant occupational implications or weight loss would benefit other significant obesity related co-morbidities
- HbA1c $> 58\text{mmol/mol}$ (7.5%) or greater than individually agreed threshold for intensification

Yes

Only to be initiated by a diabetes specialist (Consultant or GPwSI or appropriately trained diabetes specialist practitioner (GP, nurse or non-medical prescriber). Please follow pathways on page 3-7. Pharmacotherapy options are listed below

GLP-1 analogue options

GLP-1 RA options

Trulicity® (dulaglutide)

Liraglutide (branded generics licensed for T2DM available)

Ozempic® (injectable semaglutide)

Rybelsus® (oral semaglutide)

Joint GLP-1 RA and GIP agonist options

Mounjaro® (tirzepatide)

No

Not currently eligible for GLP-1 analogue therapy. Please see [T2DM Glycaemic Control Management Pathway](#) for alternative options

Weight management without T2DM or with T2DM not meeting NICE GLP-1 analogue prescribing criteria

If meet criteria for weight management (see SEL formulary), please refer patient to local specialist weight management services (SWMS) – either tier 3, tier 4 or pilot specialist primary care service in Lambeth, Lewisham or Southwark boroughs.

- Wegovy® (semaglutide) and liraglutide (branded generics licensed for weight management available) can only be prescribed by tier 3 or tier 4 SWMS.
- Mounjaro® (tirzepatide) can only be initiated by SWMS and the pilot specialist primary care services.

For further information see SEL formulary.

Use for other indications

GLP-1 RA and joint GLP-1 RA and GIP agonists are not currently licensed for any other indications. Consider alternative therapies

Drug discontinuations and formulary changes:

- Rybelsus 3mg, 7mg and 14mg tablets have been discontinued and replaced with new formulations with increased bioavailability.
 - 1.5mg tablets have replaced the discontinued 3mg tablet
 - 4mg tablets have replaced the discontinued 7mg tablet
 - 9mg tablets have replaced the discontinued 14mg tablet
 See [‘Rybelsus patient transition guide’](#) and healthcare professional letter on [risk of medication error due to introduction of new formulations](#) for further information
- Victoza® (liraglutide) has been discontinued however branded generic preparations of liraglutide are available, some of which are licensed for T2DM. See product literature for further information.
- Bydureon® (exenatide modified release), Byetta® (exenatide standard release) and Lyxumia® (lixisenatide) have been discontinued.

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Initiating Specialist Team					GP Practice
Pre-initiation	Initiation	1 month review (as required)	3 -4 month review	6 month review	Longer term
Ensure Patient meets NICE criteria (see flow chart 1) If history of diabetes for > 10 years: please discuss with consultant, as insulin may be required– see T2DM Glycaemic Control Management Pathway Under exceptional circumstances, GLP-1 analogue can be initiated by specialist teams outside of NICE guidance in licensed combinations. A clinical rationale must be detailed within patient notes and GP letter. Provide dietetic advice prior to initiation of GLP-1 analogue therapy.	Review HbA1c, renal profile, lipid profile, and liver function tests (LFTs) and ensure appropriate for GLP-1 analogue use. If starting Rybelsus® and patient is taking levothyroxine, also review thyroid profile (see page 4) Record baseline weight, HbA1c and BP Assess cautions, contraindications, interactions, hepatic and renal parameters (see pages 4-5) Review current anti-hyperglycaemic agents/doses (e.g. consider reduction of <i>sulfonylureas (SU) and/or insulin due to hypoglycaemia risk</i>). Review licensed combinations. SU may be withdrawn where clinically necessary. See notes overleaf re: retinopathy complications. Agree with the patient the most appropriate GLP-1 analogue (based on patient factors). Provide patient education and start therapy. (See pages 6-7 for dosing and education information). Provide 1st prescription (min. 1 month supply). Dose to be titrated by specialist teams to maintenance dose. Request ongoing prescriptions to be prescribed by GP using T2DM GLP-1 Information Sheet . If GLP-1 analogue is prescribed for patients/indications that do not meet agreed criteria, prescribing will remain with the initiating team.	Tolerability and safety: Review renal profile (see box 1), side effects, injection technique & sites/oral Rybelsus® administration, need for dose adjustment of anti-hyperglycaemic therapies, adherence with medication and lifestyle interventions If continuing GLP-1 analogue: Provide relevant patient education (see page 7), arrange 3 month HbA1c, follow up appointment and renal profile test (if not undertaken at one month). Specialist team to titrate dose if clinically appropriate. Continue to 3 month review box. If stopping therapy: refer back to T2DM Glycaemic Control Management Pathway	Tolerability and safety: Review renal profile, if not taken at month 1 (see box 1), side effects, injection technique & sites/oral Rybelsus® administration, need for dose adjustment of anti-hyperglycaemic therapies, adherence with medication and lifestyle interventions Re-check thyroid function if patient is prescribed oral Rybelsus® and levothyroxine (see page 4) Efficacy: Review weight and HbA1c If continuing GLP-1 analogue: Provide relevant patient education (see page 7), arrange for HbA1c and renal profile test at 6 months and book 6 month follow up. Specialist team to titrate dose if clinically appropriate. Continue to 6 month review box. If stopping therapy: refer back to T2DM Glycaemic Control Management Pathway	Tolerability and safety: Review renal profile (see box 1), side effects, injection technique & sites/oral Rybelsus® administration, need for dose adjustment of anti-hyperglycaemic therapies, adherence with medication and lifestyle interventions Efficacy review & continuation criteria: HbA1c reduction is >11mmol/mol (1%) or individual target HbA1c AND weight loss ≥3% of initial body If continuing GLP-1 analogue: If co-prescribed with oral anti-hyperglycaemic medication, provide relevant patient education and arrange for discharge to GP. If co-prescribed insulin +/- oral anti-hyperglycaemic medication, provide relevant patient education and ensure ongoing support from a consultant led multidisciplinary team dependent on local commissioning arrangements. If stopping therapy: refer back to T2DM Glycaemic Control Management Pathway	Review eGFR and creatinine at least annually, HbA1c six monthly, LFTs annually. Thyroid function in those taking thyroid medication and Rybelsus®. Some people may need more frequent monitoring based on patient factors. See GLP-1 analogue information sheet for more information. Review at least annually. Where HbA1c or weight increases back to pre-treatment levels or HbA1c is above individualised target despite maximised lifestyle interventions and medication compliance, or additional therapy is required in line with the T2DM glycaemic control pathway, please contact or refer back to diabetes specialist for review

Box 1: renal function advice - read in conjunction with renal advice on page 5:

- If eGFR drop >10ml/min, review eGFR trend prior to initiation. Discuss with Doctor. Consider other causes, re-check profile within 4 weeks
- If eGFR drop 5-10ml/min, re-check at 6 months and if stable check and review at 12 months (may be via GP). If not stable, discuss with Doctor
- If eGFR drop <5ml/min, re-check at 6 & 12 months (may be via GP at 12 months). Discuss with Doctor if not stable

Pathway notes:

- For people meeting glucose targets on GLP-1 analogues in combinations previously recognised by NICE, therapy can be continued. Ensure therapy remains effective.
- People stabilised on injectable GLP-1 analogues should not be switched over to oral Rybelsus® unless there is a robust clinical rationale to do so e.g. needle phobia, administration issues, shortage of injectable GLP-1 analogues. Please refer to the [Summary of Product Characteristics \(SPC\)](#) for information on changing between preparations. Injectable therapy ideally would be 1st line therapy when using a GLP-1 analogue.

Contra-indications and cautions*



Not recommended	Contra-indications	Cautions
- Acute pancreatitis - Pregnancy or breast feeding or those considering pregnancy - For treatment of diabetic ketoacidosis (DKA) - Type 1 diabetes - Severe gastrointestinal (GI) disease e.g. gastroparesis (tirzepatide states caution)	- Hypersensitivity to active substance or excipients - Pre-clinical studies in rats/mice showed an increase in thyroid c-cell tumours, human relevance is considered low but cannot be excluded. Avoid in personal or family history of medullary thyroid carcinoma and in those with multiple endocrine neoplasia syndrome type 2 (MEN 2)	- History of pancreatitis - Risk factors for pancreatitis e.g. high alcohol intake, gall bladder or biliary disease, high triglycerides - Limited/very limited experience in those aged ≥ 75 years (See SPC for further information). - Diabetic retinopathy: rapid improvement in glucose control (e.g. with insulin and GLP-1 analogues) has been associated with temporary worsening of diabetic retinopathy. Review recent retinopathy screening report prior to initiation and monitor closely for all patients. - DKA has been reported in association with some GLP-1 analogues, particularly after discontinuation or reduction of concomitant insulin. If insulin dose is to be reduced, undertake in a stepwise manner with blood glucose self-monitoring. Discuss risk factors for and signs and symptoms of DKA and advise to seek immediate medical advice if these develop. - Cases of pulmonary aspiration have been reported in patients receiving GLP-1 receptor agonists undergoing general anaesthesia or deep sedation. Therefore, the increased risk of residual gastric content due to delayed gastric emptying should be considered prior to performing procedures with general anaesthesia or deep sedation.

LIRAGLUTIDE (BRANDED GENERICS FOR T2DM AVAILABLE) INJECTION	- Not recommended: (1) Heart failure NYHA IV (2) Patients with inflammatory bowel disease - Caution: pre-existing thyroid disease
TRULICITY®(DULAGLUTIDE) INJECTION	- Other: (1) For those receiving oral medicinal products requiring rapid GI absorption or prolonged release formulations, the potential for altered drug exposure should be considered, particularly at the time of dulaglutide treatment initiation.
OZEMPIC® (SEMAGLUTIDE) INJECTION	- Not recommended: Heart failure NYHA IV - Caution: (1) Those with diabetic retinopathy (DR) treated with insulin: increased risk of developing DR complications. Caution should be exercised when using semaglutide in patients with DR treated with insulin. Monitor closely. Rapid improvement in glucose control has been associated with temporary worsening of DR, but other mechanisms cannot be excluded. (2) Those receiving oral medicinal products requiring rapid GI absorption. - Other: (1). If pregnancy occurs, semaglutide should be discontinued. Discontinue at least 2 months before a planned pregnancy due to the long half-life.
RYBELSUS® (SEMAGLUTIDE) ORAL TABLET	- Not recommended: (1) Heart failure NYHA IV. (2) There is no therapeutic experience in patients with bariatric surgery. - Caution: Those with DR treated with insulin and injectable semaglutide (risk cannot be excluded for oral semaglutide): increased risk of developing DR complications. Monitor closely. Rapid improvement in glucose control has been associated with temporary worsening of DR, but other mechanisms cannot be excluded. - Other: (1) Compliance with the dosing regimen is recommended for optimal effect. If treatment response lower than expected, be aware that the absorption of oral semaglutide is highly variable and may be minimal. (2) Delays gastric emptying which may influence the absorption of other oral medicinal products. (3) Total exposure of thyroxine was increased by 33% following a single dose of levothyroxine. Monitoring of thyroid parameters need to be considered when treating with semaglutide at the same time as levothyroxine, monitor thyroid function tests 6-8 weeks after initiation (4) If pregnancy occurs, semaglutide should be discontinued. Discontinued at least 2 months before a planned pregnancy due to the long half-life.
MOUNJARO® ▼ (TIRZEPATIDE) INJECTION	- Caution: (1) Not been studied in patients with severe gastrointestinal disease including severe gastroparesis. (2) Not been studied in people with non-proliferative DR requiring acute therapy, proliferative DR or diabetic macular oedema. Use with caution with appropriate monitoring. - Other: (1) Very limited data in people aged ≥ 85 years. (2) Preparation contains benzyl alcohol. May cause allergic reactions. People with hepatic or renal impairment should be informed of the potential risk of metabolic acidosis due to accumulation of benzyl alcohol over time. (3) Delays gastric emptying and has the potential to impact the rate of absorption of concomitantly administered oral medicines. Effects are most pronounced at the time of tirzepatide initiation. Recommended to monitor those on oral medicines with narrow therapeutic index (e.g. warfarin, digoxin) especially at tirzepatide initiation and dose increase. Risk of delayed effect to be considered for oral medicines where a rapid onset of effect is important. (4) Limited information on efficacy of oral contraceptives (OCP) with tirzepatide use. Reduced efficacy of OCPs cannot be excluded therefore it is advised switching to a non-oral contraceptive method, or add a barrier method of contraception upon initiating tirzepatide therapy (for 4 weeks), or after each dose escalation (for 4 weeks) (5) Tirzepatide is not recommended in pregnancy and women of childbearing potential not using contraception. Discontinued at least 1 month before a planned pregnancy due to the long half-life (6) It is unknown whether tirzepatide is excreted in human milk a risk benefit decision must be made whether to stop tirzepatide or stop breastfeeding.

*Please note: information is not exhaustive, please see Summary of Product Characteristics (SPC) at www.medicines.org.uk for more information including details of interaction with other medicinal products.

	HEPATIC IMPAIRMENT	RENAL IMPAIRMENT
LIRAGLUTIDE (BRANDED GENERICS LICENSED FOR T2DM AVAILABLE) INJECTION	- No dose adjustment recommended in mild or moderate hepatic impairment. - Not recommended in severe hepatic impairment	- No dose adjustment in mild, moderate or severe renal impairment - Not recommended for end stage renal disease (<15ml/min)
TRULICITY® (DULAGLUTIDE) INJECTION	No dose adjustment required in hepatic impairment.	- No dose adjustment in mild, moderate or severe renal impairment - Not recommended for end stage renal disease (<15ml/min)
OZEMPIC® (SEMAGLUTIDE) INJECTION	No dose adjustment required in hepatic impairment. Experience in severe hepatic impairment is limited – exercise caution if used	- No dose adjustment in mild, moderate or severe renal impairment. Experience in severe renal impairment is limited - Not recommended for end stage renal disease (<15ml/min)
RYBELSUS® (SEMAGLUTIDE) ORAL TABLET	No dose adjustment required in hepatic impairment. Experience in severe hepatic impairment is limited – exercise caution if used	- No dose adjustment in mild, moderate or severe renal impairment. Experience in severe renal impairment is limited - Not recommended for end stage renal disease (<15ml/min)
MOUNJARO® ▼ (TIRZEPATIDE) INJECTION	No dose adjustment required in hepatic impairment. Experience in severe hepatic impairment is limited – exercise caution if used	No dose adjustment in renal impairment including end stage renal disease (ESRD). Experience in severe renal impairment and ESRD is limited – exercise caution if used

Side effects *

- Hypoglycaemia:** consider dose reduction of concomitant medications to prevent hypos (in particular SU and insulin).
- Gastrointestinal effects:** nausea, vomiting, diarrhoea, constipation, abdominal pain listed as very common/common. Nausea likely at initiation and decreases over time. Caution with dehydration and renal function decline – advise on potential for dehydration and take precautions to avoid fluid depletion
- Reduced appetite**
- Diabetic retinopathy complications:** rapid improvement in glucose control (e.g. with insulin and GLP-1 analogues) has been associated with temporary worsening of diabetic retinopathy. Advise patients to immediately report any symptoms of worsening retinopathy e.g. worsening vision (gradual or sudden), sudden vision loss, shapes floating in the field of vision (floaters), blurred or patchy vision, or eye pain.
- Pancreatitis:** counsel on characteristic symptoms and action to take e.g. persistent, severe abdominal pain (sometimes radiating to the back). Patient to discontinue treatment and contact healthcare professional immediately
- Possible changes to international normalised ratio (INR) in patients on warfarin or coumarin derivatives.** More frequent monitoring recommended e.g. at initiation, dose change and cessation of liraglutide, semaglutide and tirzepatide.
- Renal function decline:** monitor as stated overleaf or more frequently if clinically indicated
- Rapid weight loss:** monitor patients for signs and symptoms of cholelithiasis
- Injection site reaction:** assess technique and ensure site rotation
- Headache**
- Increase in heart rate and tachycardia**
- Hypersensitivity**
- Small reduction in blood pressure**
- Cholelithiasis**
- Dizziness**

Note: For established medicines, report all serious suspected adverse drug reactions (ADRs) even if effect is well recognised. For black triangle drugs (▼), report all suspected ADRs. Report to <https://yellowcard.mhra.gov.uk/>

	Liraglutide (branded generics for T2DM available) injection	Trulicity® (dulaglutide) injection	Ozempic® (semaglutide) injection	Rybelsus® (semaglutide) oral tablets	Mounjaro® (tirzepatide) injection
Initiating dose	Start 0.6mg daily.	1.5mg once weekly as part of add on therapy.	0.25mg once weekly	1.5mg daily	2.5mg once weekly
Dose titration	Increase the dose to 1.2mg daily after at least one week. Dose may be increased to 1.8mg after a further week to improve glycaemic control. Dose over 1.8mg is not recommended.	If needed, the dose can be increased to 3mg once weekly after at least 4 weeks and after a further 4 weeks to 4.5mg to improve glycaemic control.	Increase the dose to 0.5mg weekly after 4 weeks. After at least a further 4 weeks, the dose can be increased to 1mg weekly to further improve glycaemic control	Increase dose to 4mg daily after 1 month. After at least a further 1 month the dose can be increased to 9mg daily to further improve glycaemic control. Maximum dose is 9 mg daily. Rybelsus should always be taken as one tablet per day. Taking more than one tablet a day should not be done to achieve the effect of a higher dose. To note: Rybelsus 3mg, 7mg and 14mg tablets have been discontinued. For further information, see page 2 above	Increase the dose to 5mg once weekly after 4 weeks as maintenance dose. The majority of glucose lowering effect (HbA1c reduction) is seen at the 5mg dose. If HbA1c target not achieved or further weight reduction required to benefit diabetes treatment further dose increases can be considered but should not be routine. Dose increases can be made in 2.5 mg increments after a minimum of 4 weeks on the current dose. Maximum dose is 15mg once a week. The recommended maintenance doses are 5, 10 and 15mg.
Administration time	Administer once daily at any time of day independent of meals, but preferably at the same time of day	Administer any time of day, with or without meals	Administer once weekly at anytime of day, with or without meals	Take once daily on an empty stomach after a recommended fasting period of at least 8 hours. Swallow tablet whole with a sip of water (up to half a glass of water equivalent to 120 ml). Wait at least 30 minutes before eating or drinking or taking other oral medicinal products to ensure full absorption.	Administer once weekly at anytime of day, with or without meals
Missed dose		Administer the missed dose as soon as possible if ≥72 hours until the next dose. If <72 hours, skip missed dose. Administer next dose on regular scheduled day	Administer as soon as possible and within 5 days after the missed dose. If >5 days, skip missed dose. Next dose to be administered on regular scheduled day.	The missed dose should be skipped and the next dose should be taken the following day.	Administer as soon as possible within 4 days of the missed dose. If >4 days, skip the missed dose. Next dose to be administered on regular scheduled day
Change in administration time		Day of weekly injection can be changed as long as last dose given ≥72hrs before	Day of weekly injection can be changed as long as the time between two doses is at least 3 days (>72hrs)		Day of weekly injection can be changes as long as the time between two doses is at least 3 days
CV benefit	Yes	Yes	Yes	Yes	Yes
No. doses in single pen	30 doses of 0.6mg 15 doses of 1.2mg 10 doses of 1.8mg	Single weekly dose	4	Not applicable	4
No. pens required each month	Between 1-3 pens dependent on dose (30 days)	Four (28 days supply)	One (28 days)	Not applicable	One (28 days)
Pen needles provided in pack?	No	Yes	Yes	Not applicable	No
Injection sites	Abdomen, thigh or upper arm	Abdomen, thigh or upper arm	Abdomen, thigh or upper arm	Not applicable	Abdomen, thigh or upper arm

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Patient education*

- Lifestyle interventions to support therapy and need for HbA1c & weight reduction for continuation at 6 months
- Dose, timing of dose, missed dose & sick day rules (see Sick Day Rules guidance)
- Blood glucose monitoring requirements (including driving in line with Driver and Vehicle Licensing Agency (DVLA) guidance)
- Hypoglycaemia risk and actions to be taken e.g., dose reduction of concomitant medications (in particular insulin & sulfonylureas (SU))
- Hypoglycaemia management
- Side effects (see page 5)
- For injections: subcutaneous use only. Educate on injection technique, storage & safe sharps disposal
- For Rybelsus® tablet: educate on method of administration
- Ensure adequate contraception if relevant (See SPC for further information, page 4 and '[The Faculty of Sexual & Reproductive Healthcare statement: GLP-1 agonists and oral contraception](#)')
- Follow up requirements including contact details for the team
- Provision of written educational material where relevant
- Provide blood form for repeat renal profile before next appointment

References:

1. Summary of Product Characteristics for Trulicity - [TRULICITY 1.5 mg solution for injection in pre-filled pen - Summary of Product Characteristics \(SmPC\) - \(emc\) \(medicines.org.uk\)](#) last accessed 26.02.24
2. Victoza SPC - [Victoza 6 mg/ml solution for injection in pre-filled pen - Summary of Product Characteristics \(SmPC\) - \(emc\) \(medicines.org.uk\)](#) last accessed 26.02.24
3. Ozempic SPC - [Ozempic 0.25 mg solution for injection in pre-filled pen - Summary of Product Characteristics \(SmPC\) - \(emc\) \(medicines.org.uk\)](#) last accessed 26.02.24
4. Rybelsus SPC - [Rybelsus 3mg tablet - Summary of Product of Characteristics \(SmPC\) - \(emc\) \(medicines.org.uk\)](#) last accessed 29.09.25
5. Mounjaro SPC - [Mounjaro KwikPen 2.5mg solution for injection pre-filled pen - Summary of Product of Characteristics \(SmPC\) - \(emc\) \(medicines.org.uk\)](#) last accessed 28.02.24
6. NICE guideline NG28 [Type 2 diabetes in adults: management](#), June 2022.
7. MHRA guidance: [GLP-1 receptor agonists: reports of diabetic ketoacidosis when concomitant insulin was rapidly reduced or discontinued](#) 19.6.2019
8. [MHRA guidance: Reporting ADRs](#)
9. [Glucagon-like peptide-1 receptor agonists and risk of thyroid cancer: A systematic review and meta-analysis of randomized controlled trials - PubMed \(nih.gov\)](#)
10. Rybelsus SPC - [Rybelsus 1.5mg tablet - Summary of Product of Characteristics \(SmPC\) - \(emc\) \(medicines.org.uk\)](#) last accessed 29.09.25
11. Rybelsus Risk Materials - [Patient Transition Guide- Your New Rybelsus Tablets - what you need to know](#) - (emc) (medicines.org.uk) last accessed 29.09.25
12. Rybelsus Risk Materials - [Direct Healthcare Professional Communication Rybelsus® \(oral semaglutide\): risk of medication error due to introduction of new formulation with increased bioavailability](#) - (emc) (medicines.org.uk) last accessed 29.09.25

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